

patients with T-ALL developed a CNS relapse, of which one had CNS leukemia at diagnosis and the other eventually developed a combined bone marrow and CNS relapse.

**Conclusion:** In conclusion, pCRT can be avoided in most children with ALL including those with T-cell immunophenotype. Our results demonstrate an excellent CNS control of leukemia just by using IT performed by strict adherence to recommended protocols.

#### LM-1\_V1.19

#### CNS COMPLICATIONS DURING TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOBLASTIC LYMPHOMA

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**Background:** Leukemia & lymphoma together cause 41% of childhood malignancies. Acute lymphoblastic leukemia (ALL) accounts for 80% of childhood leukemia, lymphoblastic lymphoma (LL) accounts for nearly 30% of pediatric lymphomas.

The treatment of both is similar and depends on a handful of drugs with a high toxicity profile.

Current treatment outcomes have improved due to risk stratification and treatment intensification. Intensified chemotherapy targets systemic disease, as well as tumor cells from the sanctuary sites especially the CNS. This entails usage of intrathecal therapy and high dose systemic chemotherapy. This has also increased the incidence and severity of CNS complications. Around 10-20% of children develop acute neurotoxicity while receiving treatment for ALL. Others report MRI abnormalities in nearly 20% children on chemotherapy for ALL, indicating that neurological complications might be under diagnosed.

The commonly reported acute CNS complications include stroke, posterior reversible encephalopathy syndrome, peripheral neuropathy, meningitis and cerebral sinus venous thrombosis (CSVT). Long term neuroendocrine and neurocognitive decline cause substantial morbidity.

Discrimination of CNS complications secondary to infection, drug toxicity or disease per se is perplexing yet essential as treatment in each case is diametrically opposite. Neuroimaging forms an important tool in reaching a diagnosis. Management is often shrouded in doubt as no clear guidelines exist regarding reduction, delay or termination of further chemotherapy.

#### Methods:

**Objective:** To analyze the clinical and neuroradiological features of acute neurotoxicity in children diagnosed with ALL/LL and treated under the ICICLE protocol.

**Study type:** Retrospective analysis

**Study period:** 1 December 2013 to 30 June 2015

**Study place:** Single pediatric tertiary care centre, North India

#### Study population:

- 77 consecutive children aged <17 years with ALL/LL who were eligible for and treated under the ICICLE protocol.
- Diagnosis of ALL and LL was based on morphological, cytochemical, immunophenotypic and cytogenetic characteristics of bone marrow aspirates and lymph node biopsy respectively.
- All children with neurological complications during treatment were included.
- Based on clinical findings, further lumbar puncture, metabolic examination, CT scan and MRI were done.

#### Results

- Seven out of 77 children (9%) developed CNS complications during therapy. None of these 7 children had any baseline neurological disease or malignant CNS involvement. Summary is shown in table 1 and 2.
- Five of these children showed gradual improvement of which four are still on chemotherapy while one withdrew from treatment. The remaining two succumbed to their CNS complications (PRES and hypothalamic syndrome).

**Conclusion:** Intensified chemotherapy has improved survival rates for ALL/LL patients, but also the incidence and severity of CNS complications. Prompt diagnosis and treatment is essential to prevent mortality and limit long term disability

#### LM-1\_V1.20

#### CYCLIN DEPENDANT KINASE INHIBITOR 2A/B AND IKZF-1 GENE DELETIONS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background:** Cyclin dependant Kinase Inhibitorand IKZF-1 genes are tumour suppressor genes implicated in many leukemia though its role in acute lymphoblastic leukemia has not been studied much. CDKN2A/B are the cell cycle inhibitor genes while IKZF1 is an important gene lymphoid development and differentiation.

**Design and Methods:** 104 pediatric acute lymphoblastic leukemia patients were investigated for deletion of CDKN2A/2B genes and related Cytogenetic prognostic factors. CDKN2A/2B and IKZF1 deletions were investigated by MLPA SALSA kit 0335.

**Results:** CDKN2A/B deletions were seen in 19.7% of B- lineage ALL and 38.4% of T lineage ALL. 59% were bi allelic deletions. Monoallelic deletions were found in 50% of B- lineage while all the T-lineage ALL were found to be bi allelic deletions for both CDKN2a and CDKN2B genes.

**Interpretation and conclusions:** CDKN2A deletions in T-ALL were seen to be associated with higher risk group and poor prognostic outcome in T-ALL. IKZF-1 deletions were seen in 10.9% of B-ALL while no IKZF1 deletions were not seen in any of the T-ALL cases.

There was no difference in the age group while CDKN2A deletions were found to be commoner in high risk group and high leukocyte count. Analysis on survival outcome were also done. IKZF1 gene deletions were seen associated with total leukocyte count, integrated cytogenetics and minimal residual disease.

#### LM-1\_V1.21

#### A COST-EFFECTIVE, HIGH SENSITIVITY 10-COLOR SINGLE TUBE FLOW-CYTOMETRY (FC) BASED B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (BCPALL) MINIMAL RESIDUAL DISEASE (MRD) ASSAY

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**Introduction:** Minimal residual disease (MRD) has been proven to be the most important indicator of relapse in BCPALL. Currently, it is widely used to monitor the treatment effectiveness and MRD -based risk stratification. Hence, the methodology for MRD assessment needs to be fast, highly sensitive and most importantly, affordable & widely applicable. Studies have shown that flow-cytometry based MRD (FC-MRD) technique cannot reach beyond the 1 in 10<sup>4</sup> sensitivity and PCR-based MRD monitoring technique is more sensitive. However, PCR based MRD assay is expensive, time consuming, laborious and has lower applicability. We present a study of the cost-effective high-sensitivity 10-color single tube FC-MRD assay in BCPALL. **Methods:** We studied 130 cases of pediatric (<15 year) BCPALL diagnosed as per WHO criteria. FC-immunophenotyping was performed on Navios flow-cytometer using bulk-lysis-and-stain method and data was analyzed with Kaluza-software. MRD was monitored in 164 bone-marrow (BM) samples at post-induction (PI, day 29-35), post-consolidation (PC, day-90) and subsequent follow-up time-points (SFU) using 10-color single tube FC-MRD assay with an additional 4-color nuclear-dye (SYTO13) tube (Table 1). Samples with cluster of ≥20 and ≥2 leukemia associated phenotypes (LAIPs) were called MRD-positive. Wherever possible, high number of events (>1.5 million) were acquired. To evaluate the applicability of assay, number of LAIPs were determined in diagnostic and MRD samples and post-induction modulation of antigen-expression was also studied.

**Results:** We studied 130 pediatric (<15 year) BCPALL cases for FC-MRD monitoring. High number of events were acquired for MRD-assay with median-events 2341500 (range, 218000 to 3152800). Of 164, MRD was positive in 69 (42%) samples with median of 0.135% and range of 0.0006% to 48.3%. We categorized positive MRD results into samples with MRD <0.001%, 0.001- <0.01%, 0.01- <0.1%, 0.1- <1.0%, 1.0- <10% and >10% and they were respectively 2.4%, 7.1%, 34.5%, 27.4%, 14.3%, and 14.3%. Of 164